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=> b reg
FILE 'REGISTRY' ENTERED AT 10:27:31 ON 24 AUG 2007
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STRUCTURE FILE UPDATES:   23 AUG 2007  HIGHEST RN 945525-31-5
DICTIONARY FILE UPDATES:  23 AUG 2007  HIGHEST RN 945525-31-5

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TSCA INFORMATION NOW CURRENT THROUGH June 29, 2007

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on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

=> d que sta l13
L2              STR
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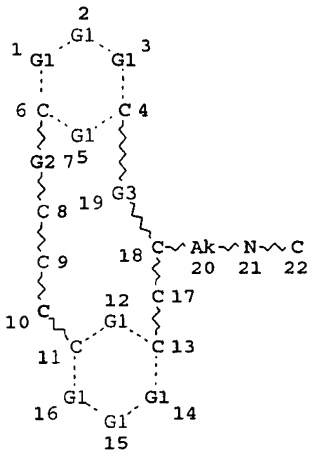


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VAR G2=C/O
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DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  22

STEREO ATTRIBUTES: NONE
L10         6149 SEA FILE=REGISTRY ABB=ON  PLU=ON  (6-6-14 OR 6-6-15)/SZ
L13           34 SEA FILE=REGISTRY SUB=L10 SSS FUL L2

100.0% PROCESSED    4161 ITERATIONS                          34 ANSWERS
SEARCH TIME: 00.00.01


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FILE 'USPATFULL' ENTERED AT 10:27:38 ON 24 AUG 2007
CA INDEXING COPYRIGHT (C) 2007 AMERICAN CHEMICAL SOCIETY (ACS)
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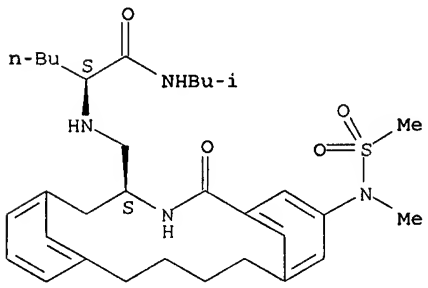
FILE 'USPAT2' ENTERED AT 10:27:38 ON 24 AUG 2007
CA INDEXING COPYRIGHT (C) 2007 AMERICAN CHEMICAL SOCIETY (ACS)

=> d bib abs hitrn fhitstr l16 tot

L16 ANSWER 1 OF 1 USPATFULL on STN
AN 2007:43085 USPATFULL
TI Macrocyclic beta-secretase inhibitors for the treatment of alzheimer's disease
IN Coburn, Craig A., Royersford, PA, UNITED STATES
Stachel, Shawn J., Perkasie, PA, UNITED STATES
Vacca, Joseph P., Telford, NJ, UNITED STATES
PI US-20070037784 A1 20070215
AI 2004US-000568153 A1 20040810 (10)
2004WO-US00025791 20040810
20060213 PCT 371 date
PRAI 2003US-000495667P 20030814 (60)
DT Utility
FS APPLICATION
LREP MERCK AND CO., INC, P O BOX 2000, RAHWAY, NJ, 07065-0907, US
CLMN Number of Claims: 17
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 859
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention is directed to compounds of formula I which are inhibitors of the beta-secretase enzyme and that are useful in the treatment or prevention of diseases in which the beta-secretase enzyme is involved, such as Alzheimer's disease. The invention is also directed to pharmaceutical compositions comprising these compounds and the use of these compounds and compositions in the prevention or treatment of such diseases in which the beta-secretase enzyme is involved. ##STR1##

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **847157-12-4P 847157-13-5P 847157-14-6P**
847157-15-7P 847157-16-8P 847157-17-9P
847157-18-0P 847157-19-1P 847157-20-4P
847157-21-5P 847157-22-6P 847157-23-7P
847157-24-8P 847157-25-9P 847157-26-0P
847157-28-2P 847157-30-6P 847157-31-7P
847157-32-8P 847157-33-9P 847157-34-0P
847157-35-1P 847157-36-2P 847157-37-3P
847157-38-4P 847157-39-5P 847157-40-8P
847157-41-9P 847157-42-0P 847157-43-1P
847157-44-2P 847157-45-3P 847157-46-4P
847225-40-5P
(preparation of macrocyclic β-secretase inhibitors for treatment of Alzheimer's disease)
IT **847157-12-4P**
(preparation of macrocyclic β-secretase inhibitors for treatment of Alzheimer's disease)
RN 847157-12-4 USPATFULL
CN Hexanamide, 2-[[[(4S)-17-[methyl(methylsulfonyl)amino]-2-oxo-3-azatricyclo[13.3.1.16,10]eicosa-1(19),6,8,10(20),15,17-hexaen-4-yl]methyl]amino]-N-(2-methylpropyl)-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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FILE 'HCAPLUS' ENTERED AT 10:27:54 ON 24 AUG 2007
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FILE COVERS 1907 - 24 Aug 2007 VOL 147 ISS 10
FILE LAST UPDATED: 23 Aug 2007 (20070823/ED)

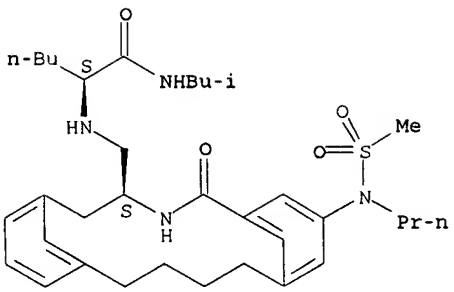
New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate
substance identification.

=> d bib abs hitstr l17 1-2

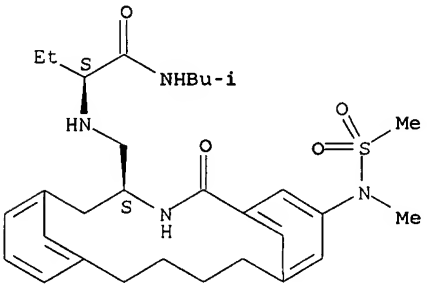
L17 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:1149497 HCAPLUS
DN 146:19371
TI Macrocyclic Inhibitors of β-Secretase: Functional Activity in an Animal Model. [Erratum to document cited in CA145:465146]
AU Stachel, Shawn J.; Coburn, Craig A.; Sankaranarayanan, Sethu; Price, Eric A.; Wu, Guoxin; Crouthamel, Michelle; Pietrak, Beth L.; Huang, Qian; Lineberger, Janet; Espeseth, Amy S.; Jin, Lixia; Ellis, Joan; Holloway, M. Katharine; Munshi, Sanjeev; Allison, Timothy; Hazuda, Daria; Simon, Adam J.; Graham, Samuel L.; Vacca, Joseph P.
CS Department of Medicinal Chemistry, Biological Chemistry, Molecular Systems and Structural Biology, Merck Research Laboratories, West Point, PA, 19486, USA
SO Journal of Medicinal Chemistry (2006), 49(24), 7252
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
AB Guoxin Wu and Michelle Crouthamel were inadvertently omitted from the author list. Their affiliation is the Department of Biol. Chemical, represented by the double dagger symbol in the paper. The correct author list is given.
IT **847157-19-1P 847157-32-8P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(macrocyclic inhibitors of β-secretase and functional activity in an animal model (Erratum))
RN 847157-19-1 HCAPLUS
CN Hexanamide, N-(2-methylpropyl)-2-[[[(4S)-17-[(methylsulfonyl)propylamino]-2-oxo-3-azatricyclo[13.3.1.16,10]eicosa-1(19),6,8,10(20),15,17-hexaen-4-yl]methyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



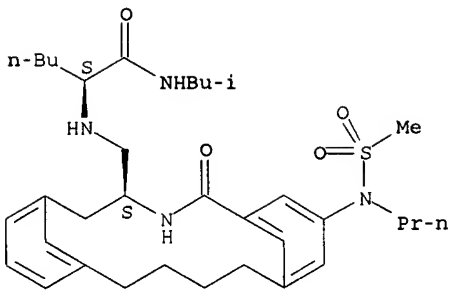
RN 847157-32-8 HCAPLUS
CN Butanamide, 2-[[[(4S)-17-[methyl(methylsulfonyl)amino]-2-oxo-3-azatricyclo[13.3.1.16,10]eicosa-1(19),6,8,10(20),15,17-hexaen-4-yl]methyl]amino]-N-(2-methylpropyl)-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



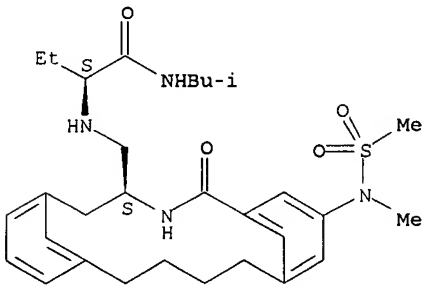
L17 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:908572 HCAPLUS
DN 145:465146
TI Macrocyclic Inhibitors of β-Secretase: Functional Activity in an Animal Model
AU Stachel, Shawn J.; Coburn, Craig A.; Sankaranarayanan, Sethu; Price, Eric A.; Pietrak, Beth L.; Huang, Qian; Lineberger, Janet; Espeseth, Amy S.; Jin, Lixia; Ellis, Joan; Holloway, M. Katharine; Munshi, Sanjeev; Allison, Timothy; Hazuda, Daria; Simon, Adam J.; Graham, Samuel L.; Vacca, Joseph P.
CS Department of Medicinal Chemistry, Biological Chemistry, Molecular Systems and Structural Biology, Merck Research Laboratories, West Point, PA, 19486, USA
SO Journal of Medicinal Chemistry (2006), 49(21), 6147-6150
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
OS CASREACT 145:465146
AB A macrocyclic inhibitor of β-secretase was designed by covalently crosslinking the P1 and P3 side chains of an isophthalamide-based inhibitor. Macrocyclization resulted in significantly improved potency and phys. properties when compared to the initial lead structures. More importantly, these macrocyclic inhibitors also displayed in vivo amyloid lowering when dosed in a murine model.
IT **847157-19-1P 847157-32-8P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(macrocyclic inhibitors of β-secretase and functional activity in an animal model)
RN 847157-19-1 HCAPLUS
CN Hexanamide, N-(2-methylpropyl)-2-[[[(4S)-17-[(methylsulfonyl)propylamino]-2-oxo-3-azatricyclo[13.3.1.16,10]eicosa-1(19),6,8,10(20),15,17-hexaen-4-yl]methyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



RN 847157-32-8 HCAPLUS
CN Butanamide, 2-[[[(4S)-17-[methyl(methylsulfonyl)amino]-2-oxo-3-azatricyclo[13.3.1.16,10]eicosa-1(19),6,8,10(20),15,17-hexaen-4-yl]methyl]amino]-N-(2-methylpropyl)-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d bib abs hitrn fhitstr l17 3

L17 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:177829 HCAPLUS
DN 142:280070
TI Preparation of macrocyclic β-secretase inhibitors for the treatment of Alzheimer's disease
IN Coburn, Craig; Stachel, Shawn J.; Vacca, Joseph P.
PA Merck & Co., Inc., USA
SO PCT Int. Appl., 42 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO2005018545	A2	20050303	2004WO-US25791	20040810
WO2005018545	A3	20050519		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU2004266605	A1	20050303	2004AU-0266605	20040810
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EP---1656359	A2	20060517	2004EP-0780598	20040810
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				

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	JP2007502278	T	20070208	2006JP-0523290	20040810
	IN2006DN00522	A	20070810	2006IN-DN00522	20060131
	US2007037784	A1	20070215	2006US-0568153	20060213
PRAI	2003US-495667P	P	20030814		
	2004WO-US25791	W	20040810		

OS CASREACT 142:280070; MARPAT 142:280070

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Macrocyclic compds. of formula I [R1 = H, R4-S(O)pN(R5), CN, etc.; R2, R3 = H, alkyl, halo, OH, alkoxy, etc.; R4 = alkyl, (substituted) NH2, Ph, benzyl, etc.; R5 = H, alkyl, Ph, benzyl; p = 0-2; X = CH2, O] are prepared which are inhibitors of the β-secretase enzyme and that are useful in the treatment or prevention of diseases such as Alzheimer's disease. The invention is also directed to pharmaceutical compns. comprising these compds. and the use of these compds. and compns. in the prevention or treatment of such diseases in which the β-secretase enzyme is involved. Thus, II was prepared from Me 3-nitrobenzoate, allyltributyl stannane, m-allyltyrosine Me ester hydrochloride and N-isobutyl-L-norleucineamide hydrochloride in several steps. The compds. had IC50 from about 1 nM to 1 μM against β-secretase enzyme.

IT **847157-12-4P 847157-13-5P 847157-14-6P**
847157-15-7P 847157-16-8P 847157-17-9P
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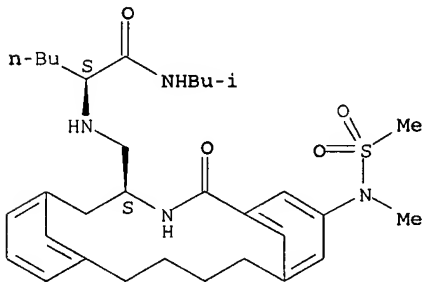
847157-32-8P 847157-33-9P 847157-34-0P
847157-35-1P 847157-36-2P 847157-37-3P
847157-38-4P 847157-39-5P 847157-40-8P
847157-41-9P 847157-42-0P 847157-43-1P
847157-44-2P 847157-45-3P 847157-46-4P
847225-40-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of macrocyclic β-secretase inhibitors for treatment of Alzheimer's disease)

IT **847157-12-4P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of macrocyclic β-secretase inhibitors for treatment of Alzheimer's disease)

RN 847157-12-4 HCAPLUS

CN Hexanamide, 2-[[[(4S)-17-[methyl(methylsulfonyl)amino]-2-oxo-3-azatricyclo[13.3.1.16,10]eicosa-1(19),6,8,10(20),15,17-hexaen-4-yl]methyl]amino]-N-(2-methylpropyl)-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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L2             STR L1
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L7             STR L2
L8           0 L7
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L10       6149 (6-6-14 OR 6-6-15)/SZ
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L12         38 L10 AND L6
L13         34 L2 FULL SUB=L10
L14         34 L13 AND L6

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L17          3 L13

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L19          0 L13

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L20          0 L13

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